DIET-EXERCISE IN PREVENTION AND TREATMENT OF METABOLIC SYNDROME
Faculty/Presenter Disclosure

- **Consultant**: Abbot Inc.
- Consultant: Seaford Inc.
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Disclosure of Commercial Support

- This program has received NO Commercial support
- This program has received NO in-kind support

- **Potential for conflict(s) of interest:**
  - Not Applicable
Mitigating Potential Bias

- Not Applicable
HOW AGING AFFECTS BELT HEIGHT...

YOUTH  ADULT  MIDDLE-AGE  OLD AGE
The Cause of Disease and Death in the Western World: The Metabolic Syndrome and infirmity

Basis of the Metabolic Syndrome

Epigenetic Trait
Environmentally acquired then heritable

Insulin resistance

Basis of Infirmity

Sarcopenia
Insulin Resistance

• Protects against malnutrition and death during Famine
• During times of Plentiful Food Results in:
  – Obesity
  – Hyperglycemia
  – Hyperlipidemia
  – Hypertension
  – inflammation
Insulin Resistant State

Carbohydrate intake → Blood Glucose

Blood Glucose → Insulin secretion

Insulin secretion → Glycogen Synthesis

Glycogen Synthesis → Adipose Tissue

Adipose Tissue → Muscle cell
EFFECT OF INSULIN RESISTANCE

- INCREASED BODY FAT (OBESITY)
- DEPLETED MUSCLE GLYCOGEN (FATIGUE)
- INCREASED OXIDATIVE STRESS (INFLAMMATION)
<table>
<thead>
<tr>
<th>#</th>
<th>CHARACTERISTICS OF THE METABOLIC SYNDROME</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fasting Blood Glucose $\geq$ 5.6 mmol/L or receiving pharmacotherapy</td>
</tr>
<tr>
<td>2</td>
<td>Blood Pressure of $\geq$ 130/85 mm Hg or receiving pharmacotherapy.</td>
</tr>
<tr>
<td>3</td>
<td>Triglyceride of $\geq$ 1.7 mmol/L or receiving pharmacotherapy.</td>
</tr>
<tr>
<td>4</td>
<td>HDL-C $&lt; 1.0$ mmol/L Males and $&lt; 1.3$ mmol/L females</td>
</tr>
<tr>
<td>5</td>
<td>Abdominal circumference as determined by a pre-specified technique:</td>
</tr>
<tr>
<td></td>
<td>- Europids, Whites, sub-Saharan Africans, Mediterranean, middle east (Arab) $\geq$ 94 cm Males, 80 cm Female.</td>
</tr>
<tr>
<td></td>
<td>- Asian and South Central Americans $\geq$ 90 cm males and 80 cm females</td>
</tr>
<tr>
<td></td>
<td>- US and Canadian Whites $\geq$ 102 cm Males, 88 cm females.</td>
</tr>
</tbody>
</table>
WHAT ABOUT OBESITY ??

FB. Ortega, D-c Lee, PT. Katzmarzyk, JR. Ruiz
The intriguing metabolically healthy but obese phenotype: cardiovascular prognosis and role of fitness.
European Heart J Sept 4 (epub ahead of print).

Sharma AM, Kushner RF. A proposed clinical staging system for obesity.
Int J Obes (Lond) 2009;33:289–295
WHAT ABOUT OBESITY??

- Increased Mortality Adjusted for Fitness

![Bar chart](Image)
WHAT ABOUT OBESITY ??

Once fitness is duly accounted for:

The metabolically healthy but obese person has a benign condition.

The metabolically abnormal obese person has a 30-50% increased mortality.

No difference in the prognosis is observed between metabolically healthy but obese individuals and metabolically healthy normal-fat individual once fitness is accounted for.

There is a key role of fitness in these associations.
IS LIFESTYLE INTERVENTION BETTER THEN DRUGS?
REDUCTION IN THE INCIDENCE OF TYPE 2 DIABETES WITH LIFESTYLE INTERVENTION OR METFORMIN: NEJM 2002:346:393-403

• 3234 nondiabetic persons with elevated fasting and post-load plasma glucose concentrations

• Randomized to placebo,
  – metformin (850 mg twice daily)
  – lifestyle-modification program
    • Goals of at least a 7 percent weight loss and
    • At least 150 minutes of physical activity per week.
REDUCTION IN THE INCIDENCE OF TYPE 2 DIABETES WITH LIFESTYLE INTERVENTION OR METFORMIN: NEJM 2002:346:393-403

Figure 2. Cumulative Incidence of Diabetes According to Study Group.
Percutaneous Coronary Angioplasty Compared With Exercise Training in Patients With Stable Coronary Artery Disease
A Randomized Trial

Rainer Hambrecht, MD; Claudia Walther, MD; Sven Möbius-Winkler, MD; Stephan Gielen, MD; Axel Linke, MD; Katrin Conradi, MD; Sandra Erbs, MD; Regine Kluge, MD; Kai Kendziorra, MD; Osama Sabri, MD; Peter Sick, MD; Gerhard Schuler, MD

EXERCISE vs ANGIOPLASTY

Circulation 2004;109:1371-1378

- 101 Patients randomized to Angioplasty or exercise protocol
- > 75% stenosis with Class I-III Angina
- Demonstrated Ischemia by Stress or Nuclear Scintigraphy
- Maximal Medical therapy matched both groups
- Triple Vessel disease in 18%
Exercise vs Angioplasty
Primary Prevention of Cardiovascular Disease with a Mediterranean Diet
NEJM 2013;368:1279-90

• 7447 patients randomized to:
  – Conventional Diet but reduce fats
  – Mediterranean Diet + Extra Virgin Olive Oli
  – Mediterranean Diet + Nuts

• Patients Had:
  – type 2 diabetes mellitus or at least three of the following major risk factors:
    • smoking,
    • Hypertension
    • elevated low-density lipoprotein
    • low high-density lipoprotein
    • overweight or obesity
    • family history of premature coronary heart disease.
<table>
<thead>
<tr>
<th>Food</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mediterranean diet</td>
<td></td>
</tr>
<tr>
<td>Recommended</td>
<td></td>
</tr>
<tr>
<td>Olive oil*</td>
<td>≥4 tbsp/day</td>
</tr>
<tr>
<td>Tree nuts and peanuts†</td>
<td>≥3 servings/wk</td>
</tr>
<tr>
<td>Fresh fruits</td>
<td>≥3 servings/day</td>
</tr>
<tr>
<td>Vegetables</td>
<td>≥2 servings/day</td>
</tr>
<tr>
<td>Fish (especially fatty fish), seafood</td>
<td>≥3 servings/wk</td>
</tr>
<tr>
<td>Legumes</td>
<td>≥3 servings/wk</td>
</tr>
<tr>
<td>Sofrito‡</td>
<td>≥2 servings/wk</td>
</tr>
<tr>
<td>White meat</td>
<td>Instead of red meat</td>
</tr>
<tr>
<td>Wine with meals (optionally, only for habitual drinkers)</td>
<td>≥7 glasses/wk</td>
</tr>
<tr>
<td>Discouraged</td>
<td></td>
</tr>
<tr>
<td>Soda drinks</td>
<td>&lt;1 drink/day</td>
</tr>
<tr>
<td>Commercial bakery goods, sweets, and pastries§</td>
<td>&lt;3 servings/wk</td>
</tr>
<tr>
<td>Spread fats</td>
<td>&lt;1 serving/day</td>
</tr>
<tr>
<td>Red and processed meats</td>
<td>&lt;1 serving/day</td>
</tr>
</tbody>
</table>
Mediterranean Diet VS Control

MDEVO = Mediterranean Diet with Extra virgin olive oil
MDNUTS= Mediterranean Diet with Nuts
ALL DATA except fishoil % difference from Controls  P<0.001
Fish Oil difference as g/day p<0.001

NEJM 2013;368:1279-90
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mediterranean Diet with EVOO (N = 2543)</th>
<th>Mediterranean Diet with Nuts (N = 2454)</th>
<th>Control Diet (N = 2450)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex — no. (%) Only (3)</td>
<td>1493 (58.7)</td>
<td>1326 (54.0)</td>
<td>1463 (59.7)</td>
</tr>
<tr>
<td>Age — yr†</td>
<td>67.0±6.2</td>
<td>66.7±6.1</td>
<td>67.3±6.3</td>
</tr>
<tr>
<td>Race or ethnic group — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White, from Europe</td>
<td>2470 (97.1)</td>
<td>2390 (97.4)</td>
<td>2375 (96.9)</td>
</tr>
<tr>
<td>Hispanic, from Central or South America</td>
<td>35 (1.4)</td>
<td>29 (1.2)</td>
<td>38 (1.6)</td>
</tr>
<tr>
<td>Other</td>
<td>38 (1.5)</td>
<td>35 (1.4)</td>
<td>37 (1.5)</td>
</tr>
<tr>
<td>Smoking status — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoked</td>
<td>1572 (61.8)</td>
<td>1465 (59.7)</td>
<td>1527 (62.3)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>618 (24.3)</td>
<td>634 (25.8)</td>
<td>584 (23.8)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>353 (13.9)</td>
<td>355 (14.5)</td>
<td>339 (13.8)</td>
</tr>
<tr>
<td>Body-mass index†‡‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>29.9±3.7</td>
<td>29.7±3.8</td>
<td>30.2±4.0</td>
</tr>
<tr>
<td>&lt;25 — no. (%)</td>
<td>195 (7.7)</td>
<td>204 (8.3)</td>
<td>164 (6.7)</td>
</tr>
<tr>
<td>25–30 — no. (%)</td>
<td>1153 (45.3)</td>
<td>1163 (47.4)</td>
<td>1085 (44.3)</td>
</tr>
<tr>
<td>&gt;30 — no. (%)</td>
<td>1195 (47.0)</td>
<td>1087 (44.3)</td>
<td>1201 (49.0)</td>
</tr>
<tr>
<td>Waist circumference — cm</td>
<td>100±10</td>
<td>100±11</td>
<td>101±11</td>
</tr>
<tr>
<td>Waist-to-height ratio†‡‡</td>
<td>0.63±0.06</td>
<td>0.63±0.06</td>
<td>0.63±0.07</td>
</tr>
<tr>
<td>Hypertension — no. (%)¶</td>
<td>2088 (82.1)</td>
<td>2024 (82.5)</td>
<td>2050 (83.7)</td>
</tr>
<tr>
<td>Type 2 diabetes — no. (%)¶</td>
<td>1282 (50.4)</td>
<td>1143 (46.6)</td>
<td>1189 (48.5)</td>
</tr>
<tr>
<td>Dyslipidemia — no. (%)**</td>
<td>1821 (71.6)</td>
<td>1799 (73.3)</td>
<td>1763 (72.0)</td>
</tr>
<tr>
<td>Family history of premature CHD — no. (%)‡†‡</td>
<td>576 (22.7)</td>
<td>532 (21.7)</td>
<td>560 (22.9)</td>
</tr>
</tbody>
</table>
# PRIMARY END POINT:
MI, Stroke, Death from CVS causes

<table>
<thead>
<tr>
<th>End Point</th>
<th>Mediterranean Diet with EVOO (N = 2543)</th>
<th>Mediterranean Diet with Nuts (N = 2454)</th>
<th>Control Diet (N = 2450)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hazard ratio for Mediterranean diets combined vs. control (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary end point</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>0.70 (0.55–0.89)</td>
<td>1 (ref)</td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>Multivariable-adjusted 1‡</td>
<td>0.71 (0.56–0.90)</td>
<td>1 (ref)</td>
<td></td>
<td>0.004</td>
</tr>
<tr>
<td>Multivariable-adjusted 2¶</td>
<td>0.71 (0.56–0.90)</td>
<td>1 (ref)</td>
<td></td>
<td>0.005</td>
</tr>
</tbody>
</table>

‡ The primary end point was a composite of myocardial infarction, stroke, and death from cardiovascular causes.
§ The primary end point was stratified according to recruiting center and adjusted for sex, age (continuous variable), family history of premature coronary heart disease (yes or no), and smoking status (never smoked, former smoker, or current smoker).
¶ The primary end point was additionally adjusted for body-mass index (continuous variable), waist-to-height ratio (continuous variable), hypertension at baseline (yes or no), dyslipidemia at baseline (yes or no), and diabetes at baseline (yes or no).
† The secondary end points were stratified according to recruiting center and adjusted for sex, age (continuous variable), family history of premature coronary heart disease (yes or no), smoking status (never smoked, former smoker, or current smoker), body-mass index (continuous variable), waist-to-height ratio (continuous variable), hypertension at baseline (yes or no), dyslipidemia at baseline (yes or no), and diabetes at baseline (yes or no).
A Primary End Point (acute myocardial infarction, stroke, or death from cardiovascular causes)

- Med diet, EVOO: hazard ratio, 0.70 (95% CI, 0.53–0.91); P=0.009
- Med diet, nuts: hazard ratio, 0.70 (95% CI, 0.53–0.94); P=0.02

<table>
<thead>
<tr>
<th>Years</th>
<th>No. at Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control diet</td>
</tr>
<tr>
<td>0</td>
<td>2450</td>
</tr>
<tr>
<td>1</td>
<td>2268</td>
</tr>
<tr>
<td>2</td>
<td>2020</td>
</tr>
<tr>
<td>3</td>
<td>1583</td>
</tr>
<tr>
<td>4</td>
<td>1268</td>
</tr>
<tr>
<td>5</td>
<td>946</td>
</tr>
</tbody>
</table>
Convert Insulin Resistant to Insulin Sensitive State

AEROBIC EXERCISE

Low glycemic index diet
Exercise and Insulin resistance
1. 10 adult children of parents with NIDDM
2. 8 normal subjects
3. 6 weeks of aerobic exercise
4. Stair Climbing (aerobic)
5. 3 sessions per week
6. 45 min/session at 65% of VO2 Max
Exercise and Insulin resistance

Glycogen Synthesis
% of control at baseline

Control
Insulin Resistance

Weeks
Hypertension Exercise and Mortality
Engstrom et al. J Hypertens 17:737-42, 1999

- Cohort of 642 men followed for 25 years
- Vigorous activity 100 men BP >165/95.
TYPES OF EXERCISE

• AEROBIC EXERCISE
  – SHORT TERM
  – ENDURANCE

• RESISTIVE
  – ISOMETRIC
  – ISOTONIC
Reversal of Sarcopenic infirmity
Age enrolled 87 ± 0.6 years.

GROUPS: Placebo, Exercise, Supplement, Supplement + Exercise.

High intensity progressive resistance training of hip and Knee extensors.

Frequency 3 days/wk       Duration 10 weeks
Sessions  45 minutes

Supplement  360 Kcals/d 17% protein
Outcomes:
1. Muscle Function
2. Physical Function
3. Nutritional Intake
4. Body Composition
5. Physical Activity
Figure 2. Breakdown of healthy behavioural changes (increase physical activity and improve diet) recommended by the physicians to (A) all of their patients, (B) patients with dyslipidemia, (C) patients with type 2 diabetes mellitus (T2DM), and (D) patients with hypertension. Solo, physicians from traditional nonteam practice. † P < 0.0001 vs corresponding primary care team (PCT) data.
CHANGE

Canadian Health Advanced By Nutrition and Graded Exercise

CHANGE Health Paradigm IS CENTERED ON THE FAMILY PHYSICIAN
CHANGE SITES

- PRIMARY CARE NETWORK EDMONTON
- POLYCLINIC TORONTO
- U OF LAVAL PRIMARY CARE
Figure 2: Change in PROCAM risk compared with baseline risk. CI = confidence interval, LOESS = locally weighted regression smoothing, PROCAM = Prospective Cardiovascular Munster.
Conclusions

- **Aerobic Exercise >3 days a week 70% VO2 Max**
  - INSULIN SENSITIZE
- **Resistive Exercise Target Extensor Muscles**
  - Prevent and reduce Sarcopenia and Frailty
- **Mediterranean Diet**
  - Reduce risk of Cardiovascular Disease
Conclusions

• Totally neglected in practice except for platitudes like
  – “Balanced intake of all food groups”
  – “Go for long walks”

INDIVIDUALLY TAILORED
PROGRAM NEEDS TO BECOME
PART OF MEDICAL CARE